



PCT

RAW SEQUENCE LISTING

DATE: 12/10/2004

PATENT APPLICATION: US/10/516,505

TIME: 14:21:08

Input Set : A:\PTS-0055WO.txt

Output Set: N:\CRF4\12102004\J516505.raw

3 <110> APPLICANT: ISIS Pharmaceuticals Inc.
 4 Eric G. Marcusson
 5 C. Frank Bennett
 6 Kenneth W. Dobie
 8 <120> TITLE OF INVENTION: ANTISENSE MODULATION OF EXTRACELLULAR-SIGNAL-REGULATED
 KINASE-6 EXPRESSION
 10 <130> FILE REFERENCE: PTS-0055WO
 C--> 12 <140> CURRENT APPLICATION NUMBER: US/10/516,505
 C--> 12 <141> CURRENT FILING DATE: 2004-12-01
 12 <150> PRIOR APPLICATION NUMBER: 10/348,431
 13 <151> PRIOR FILING DATE: 2003-01-17
 15 <150> PRIOR APPLICATION NUMBER: 10/174,465
 16 <151> PRIOR FILING DATE: 2002-06-17
 18 <160> NUMBER OF SEQ ID NOS: 233
 20 <210> SEQ ID NO: 1
 21 <211> LENGTH: 20
 22 <212> TYPE: DNA
 23 <213> ORGANISM: Artificial Sequence
 25 <220> FEATURE:
 27 <223> OTHER INFORMATION: Antisense Oligonucleotide
 29 <400> SEQUENCE: 1
 30 tccgtcatcg ctcctcaggg 20
 33 <210> SEQ ID NO: 2
 34 <211> LENGTH: 20
 35 <212> TYPE: DNA
 36 <213> ORGANISM: Artificial Sequence
 38 <220> FEATURE:
 40 <223> OTHER INFORMATION: Antisense Oligonucleotide
 42 <400> SEQUENCE: 2
 43 gtgcgcgcga gcccgaaatc 20
 46 <210> SEQ ID NO: 3
 47 <211> LENGTH: 20
 48 <212> TYPE: DNA
 49 <213> ORGANISM: Artificial Sequence
 51 <220> FEATURE:
 53 <223> OTHER INFORMATION: Antisense Oligonucleotide
 55 <400> SEQUENCE: 3
 56 atgcattctg cccccaagga 20
 59 <210> SEQ ID NO: 4
 60 <211> LENGTH: 1670
 61 <212> TYPE: DNA
 62 <213> ORGANISM: H. sapiens
 64 <220> FEATURE:
 66 <220> FEATURE:

Does Not Comply
 Corrected Diskette Needed

P.6

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```

67 <221> NAME/KEY: CDS
68 <222> LOCATION: (34)...(1137)
70 <400> SEQUENCE: 4
71 ggctctgcgg ggtgggcagc tcccgggcct gcc atg agc tct ccg ccg ccc acc      54
72                                     Met Ser Ser Pro Pro Pro Thr
73                                     1           5
75 cgc agt ggc ttt tac cgc cag gag gtg acc aag acg gcc tgg gag gtg      102
76 Arg Ser Gly Phe Tyr Arg Gln Glu Val Thr Lys Thr Ala Trp Glu Val
77         10           15           20
79 cgc gcc gtg tac cgg gac ctg cag ccc gtg ggc tcg ggc gcc tac ggc      150
80 Arg Ala Val Tyr Arg Asp Leu Gln Pro Val Gly Ser Gly Ala Tyr Gly
81         25           30           35
83 gcg gtg tgc tcg gcc gtg gac ggc cgc acc ggc gct aag gtt gcc atc      198
84 Ala Val Cys Ser Ala Val Asp Gly Arg Thr Gly Ala Lys Val Ala Ile
85         40           45           50           55
87 aag aag ctg tat cgg ccc ttc cag tcc gag ctg ttc gcc aag ctc gcc      246
88 Lys Lys Leu Tyr Arg Pro Phe Gln Ser Glu Leu Phe Ala Lys Leu Ala
89         60           65           70
91 tac cgc gag ctg cgc ctg ctc aag cac atg cgc cac gag aac gtg atc      294
92 Tyr Arg Glu Leu Arg Leu Leu Lys His Met Arg His Glu Asn Val Ile
93         75           80           85
95 ggg ctg ctg gac gta ttc act cct gat gag acc ctg gat gac ttc acg      342
96 Gly Leu Leu Asp Val Phe Thr Pro Asp Glu Thr Leu Asp Asp Phe Thr
97         90           95           100
99 gac ttt tac ctg gtg atg ccg ttc atg ggc acc gac ctg ggc aag ctc      390
100 Asp Phe Tyr Leu Val Met Pro Phe Met Gly Thr Asp Leu Gly Lys Leu
101        105           110           115
103 atg aaa cat gag aag cta ggc gag gac cgg atc cag ttc ctc gtg tac      438
104 Met Lys His Glu Lys Leu Gly Glu Asp Arg Ile Gln Phe Leu Val Tyr
105        120           125           130           135
107 cag atg atg aag ggg ctg agg tat atc cac gct gcc ggc atc atc cac      486
108 Gln Met Met Lys Gly Leu Arg Tyr Ile His Ala Ala Gly Ile Ile His
109        140           145           150
111 aga gac ctg aag ccc ggc aac ctg gct gtg aac gaa gac tgt gag ctg      534
112 Arg Asp Leu Lys Pro Gly Asn Leu Ala Val Asn Glu Asp Cys Glu Leu
113        155           160           165
115 aag atc ctg gac ttc ggc ctg gcc agg cag gca gac agt gag atg act      582
116 Lys Ile Leu Asp Phe Gly Leu Ala Arg Gln Ala Asp Ser Glu Met Thr
117        170           175           180
119 ggg tac gtg gtg acc cgg tgg tac cgg gct ccc gag gtc atc ttg aat      630
120 Gly Tyr Val Val Thr Arg Trp Tyr Arg Ala Pro Glu Val Ile Leu Asn
121        185           190           195
123 tgg atc gcg tac acg cag acg gtg gac atc tgg tct gtg ggc tgc atc      678
124 Trp Ile Ala Tyr Thr Gln Thr Val Asp Ile Trp Ser Val Gly Cys Ile
125        200           205           210           215
127 atg gcg gag atg atc aca ggc aag acg ctg ttc aag ggc agc gac cac      726
128 Met Ala Glu Met Ile Thr Gly Lys Thr Leu Phe Lys Gly Ser Asp His
129        220           225           230
131 ctg gac cag ctg aag gag atc atg aag gtg acg ggg acg cct ccg gct      774

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```

132 Leu Asp Gln Leu Lys Glu Ile Met Lys Val Thr Gly Thr Pro Pro Ala
133          235          240          245
135 gag ttt gtg cag cgg ctg cag agc gat gag gcc aag aac tac atg aag      822
136 Glu Phe Val Gln Arg Leu Gln Ser Asp Glu Ala Lys Asn Tyr Met Lys
137          250          255          260
139 ggc ctc ccc gaa ttg gag aag aag gat ttt gcc tct atc ctg acc aat      870
140 Gly Leu Pro Glu Leu Glu Lys Lys Asp Phe Ala Ser Ile Leu Thr Asn
141          265          270          275
143 gca agc cct ctg gct gtg aac ctc ctg gag aag atg ctg gtg ctg gac      918
144 Ala Ser Pro Leu Ala Val Asn Leu Leu Glu Lys Met Leu Val Leu Asp
145 280          285          290          295
147 gcg gac atc agg ttg act gca ggc gag ttt ctt tcc cat ccc tac ttc      966
148 Ala Asp Ile Arg Leu Thr Ala Gly Glu Phe Leu Ser His Pro Tyr Phe
149          300          305          310
151 gag tcc ctg cac gac acg gaa gat gag ccc cag gtc cag aag tat gat      1014
152 Glu Ser Leu His Asp Thr Glu Asp Glu Pro Gln Val Gln Lys Tyr Asp
153          315          320          325
155 gac tcc ttt gac tac ttt gac cgc aca ctg gat gaa tgg aag cgt gtt      1062
156 Asp Ser Phe Asp Tyr Phe Asp Arg Thr Leu Asp Glu Trp Lys Arg Val
157          330          335          340
159 act tac aaa gag gtg ctc agc ttc aag cct ccc cgg cag ctg ggg gcc      1110
160 Thr Tyr Lys Glu Val Leu Ser Phe Lys Pro Pro Arg Gln Leu Gly Ala
161          345          350          355
163 agg gtc tcc aag gag acg cct ctg tga agatctctgg gctccggggt      1157
164 Arg Val Ser Lys Glu Thr Pro Leu
165 360          365
167 ggcagtgagg accaccttca ccttccacct gagagggggac tctcgttgcc accttgacct      1217
169 tggctggggc ttgcatccca aggcattccat cagagcagac gcccggggttc catggaccct      1277
171 cctccccact gccatgcctc tgctcttttg cgcccatcat ggaggagcac ctgaactttc      1337
173 tggacaagac ctctggccga cctgggggatg gcctctgate cctggagcag tggaacacaa      1397
175 aaaacaatac tctcagaaac ctcagagctg gtggggctcc agatcagcct tggcctctga      1457
177 gccctgcttg ctctggggcca tgcagaggaa ggacagaggg tgggagcagg gcaccaactc      1517
179 agggacatcc cctctccttg ggcagctcag tggaccttcc tgcaccccca gcctggaatg      1577
181 taaatcagct gtgtggtgcc cgcgtggctg gaaggaaata gacccttttg tagctccaaa      1637
183 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaa      1670
186 <210> SEQ ID NO: 5
187 <211> LENGTH: 20
188 <212> TYPE: DNA
189 <213> ORGANISM: Artificial Sequence
191 <220> FEATURE:
193 <223> OTHER INFORMATION: PCR Primer
195 <400> SEQUENCE: 5
196 ctcgttgcca ccttgacctt      20
199 <210> SEQ ID NO: 6
200 <211> LENGTH: 16
201 <212> TYPE: DNA
202 <213> ORGANISM: Artificial Sequence
204 <220> FEATURE:
206 <223> OTHER INFORMATION: PCR Primer

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```

208 <400> SEQUENCE: 6
209 tggaacccgg gcgtct                                16
212 <210> SEQ ID NO: 7
213 <211> LENGTH: 24
214 <212> TYPE: DNA
215 <213> ORGANISM: Artificial Sequence
217 <220> FEATURE:
219 <223> OTHER INFORMATION: PCR Probe
221 <400> SEQUENCE: 7
222 ttgcatcca aggcattcat caga                        24
225 <210> SEQ ID NO: 8
226 <211> LENGTH: 19
227 <212> TYPE: DNA
228 <213> ORGANISM: Artificial Sequence
230 <220> FEATURE:
232 <223> OTHER INFORMATION: PCR Primer
234 <400> SEQUENCE: 8
235 gaaggtgaag gtcggagtc                            19
238 <210> SEQ ID NO: 9
239 <211> LENGTH: 20
240 <212> TYPE: DNA
241 <213> ORGANISM: Artificial Sequence
243 <220> FEATURE:
245 <223> OTHER INFORMATION: PCR Primer
247 <400> SEQUENCE: 9
248 gaagatggtg atgggatttc                            20
251 <210> SEQ ID NO: 10
252 <211> LENGTH: 20
253 <212> TYPE: DNA
254 <213> ORGANISM: Artificial Sequence
256 <220> FEATURE:
258 <223> OTHER INFORMATION: PCR Probe
260 <400> SEQUENCE: 10
261 caagcttccc gttctcagcc                            20
264 <210> SEQ ID NO: 11
265 <211> LENGTH: 20
266 <212> TYPE: DNA
267 <213> ORGANISM: Artificial Sequence
269 <220> FEATURE:
271 <223> OTHER INFORMATION: Antisense Oligonucleotide
273 <400> SEQUENCE: 11
274 ccttcatcat ctggtacag                             20
277 <210> SEQ ID NO: 12
278 <211> LENGTH: 20
279 <212> TYPE: DNA
280 <213> ORGANISM: Artificial Sequence
282 <220> FEATURE:
284 <223> OTHER INFORMATION: Antisense Oligonucleotide
286 <400> SEQUENCE: 12

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RAW SEQUENCE LISTING

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287 tccttcagct ggtccaggtg                                20
290 <210> SEQ ID NO: 13
291 <211> LENGTH: 20
292 <212> TYPE: DNA
293 <213> ORGANISM: Artificial Sequence
295 <220> FEATURE:
297 <223> OTHER INFORMATION: Antisense Oligonucleotide
299 <400> SEQUENCE: 13
300 ccaccagctc tgaggtttct                                20
303 <210> SEQ ID NO: 14
304 <211> LENGTH: 20
305 <212> TYPE: DNA
306 <213> ORGANISM: Artificial Sequence
308 <220> FEATURE:
310 <223> OTHER INFORMATION: Antisense Oligonucleotide
312 <400> SEQUENCE: 14
313 ggagagctca tggcaggccc                                20
316 <210> SEQ ID NO: 15
317 <211> LENGTH: 20
318 <212> TYPE: DNA
319 <213> ORGANISM: Artificial Sequence
321 <220> FEATURE:
323 <223> OTHER INFORMATION: Antisense Oligonucleotide
325 <400> SEQUENCE: 15
326 gtggcgcatg tgcttgagca                                20
329 <210> SEQ ID NO: 16
330 <211> LENGTH: 20
331 <212> TYPE: DNA
332 <213> ORGANISM: Artificial Sequence
334 <220> FEATURE:
336 <223> OTHER INFORMATION: Antisense Oligonucleotide
338 <400> SEQUENCE: 16
339 cccttcacatca tctggtacac                                20
342 <210> SEQ ID NO: 17
343 <211> LENGTH: 20
344 <212> TYPE: DNA
345 <213> ORGANISM: Artificial Sequence
347 <220> FEATURE:
349 <223> OTHER INFORMATION: Antisense Oligonucleotide
351 <400> SEQUENCE: 17
352 atccagggtc tcatcaggag                                20
355 <210> SEQ ID NO: 18
356 <211> LENGTH: 20
357 <212> TYPE: DNA
358 <213> ORGANISM: Artificial Sequence
360 <220> FEATURE:
362 <223> OTHER INFORMATION: Antisense Oligonucleotide
364 <400> SEQUENCE: 18
365 cccggagccc agagatcttc                                20

```


10/5/6, 505

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delete at end of file

RAW SEQUENCE LISTING ERROR SUMMARY
PATENT APPLICATION: US/10/516,505

DATE: 12/10/2004
TIME: 14:21:09

Input Set : A:\PTS-0055WO.txt
Output Set: N:\CRF4\12102004\J516505.raw

Please Note:

Use of n and/or Xaa have been detected in the Sequence Listing. Please review the Sequence Listing to ensure that a corresponding explanation is presented in the <220> to <223> fields of each sequence which presents at least one n or Xaa.

Seq#:71; N Pos. 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20
Seq#:75; N Pos. 727

Invalid Line Length:

The rules require that a line not exceed 72 characters in length. This includes spaces.

Seq#:1; Line(s) 8

VERIFICATION SUMMARY

PATENT APPLICATION: US/10/516,505

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Input Set : A:\PTS-0055WO.txt

Output Set: N:\CRF4\12102004\J516505.raw

L:12 M:270 C: Current Application Number differs, Replaced Current Application No
L:12 M:271 C: Current Filing Date differs, Replaced Current Filing Date
L:1007 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:1011 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:71
L:1012 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:71 after pos.:0
L:1307 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:75,Line#:1305
L:1332 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:75 after pos.:720
L:3333 M:334 W: (2) Invalid Amino Acid in Coding Region, NUMBER OF INVALID KEYS:1
L:3335 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:233
L:3335 M:334 W: (2) Invalid Amino Acid in Coding Region, NUMBER OF INVALID KEYS:1
L:3337 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:233
L:3337 M:334 W: (2) Invalid Amino Acid in Coding Region, NUMBER OF INVALID KEYS:1
L:3339 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:233
L:3339 M:334 W: (2) Invalid Amino Acid in Coding Region, NUMBER OF INVALID KEYS:1